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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/042,406	01/09/2002	John B. Sheehan	1011U-1	9034

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2021 STIERLIN COURT
MOUNTAIN VIEW, CA 94043

EXAMINER

MAHATAN, CHANNING

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/042,406

Applicant(s)

SHEEHAN ET AL.

Examiner

Channing S Mahatan

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7,9,11-23,26 and 28-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9, 11-23, 26, and 28-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date, _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

APPLICANTS' ARGUMENTS

Applicants' arguments, filed 26 January 2004, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

CLAIMS UNDER EXAMINATION

Claims herein under examination are claims 1-7, 9, 11-23, 26, 28-32. Claims 8, 10, 24, 25, and 27 have been cancelled.

Claims Rejected Under 35 U.S.C. § 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 9, 11-23, 26, 28-32 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

VAGUE AND INDEFINITE

Claims 1, 22, 32, and all claims dependent therefrom are indefinite due to the lack of clarity of the claim language failing to recite a final process step, which agrees back with the preamble. The preamble states that it is "A method for designing primer pairs" (claim 1)/"A computer-implemented method for designing primer pairs" (claim 22)/"A system that designs primer pairs" (claim 32), however, a final step of "selecting a subset of primer pairs" is recited.

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Absent from the body of the instant claims is an indication that primer pairs are intended to be designed as recited in the preamble. While minor details are not required in method claims, at least the basic step must be recited in a positive, active fashion. The claims do not set forth the conditions/state when primer pairs are designed. Additionally, it is unclear if the instantly claimed invention is intended to be designing primer pairs or selecting primer pairs.

Clarification of the metes and bounds of the claim is requested via clearer claim wording.

Claims 1, 22, 32, and all claims dependent therefrom recites the step "removing at least selected repeat regions in said reference sequence to yield removed and unremoved reference sequence"/"removing selected repeat regions in said reference sequence to yield removed and unremoved reference sequence" which is confusing. Absence from any of the subsequent steps or dependent claims is the resulting "removed reference sequence" and therefore it is unclear what Applicants intend the resulting "removed reference sequence" to be utilized for. Further, the first selection step utilizes "said unremoved sequence", however, if no repeat regions are removed from the reference sequence then yielded unremoved sequence is the same as the reference sequence. Therefore, it is unclear what Applicants' intend the removing repeat regions step to accomplish in the instantly claimed invention. Clarification of the metes and bounds, via clearer claim language, is requested.

Claim 1 and all claims dependent therefrom recites the phrase "having reduced overlap" which is vague and indefinite. The metes and bounds of the language "reduced overlap" remains unclear as to what Applicants' intend the language to encompass, wherein the optional language type language (as amended) is unclear (refer to above 35 U.S.C. § 112 2nd Paragraph Rejection). Applicants can resolve this issue by particularly pointing out the criteria/range that encompasses

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“having reduced overlap”. Clarification of the metes and bounds, via clearer claim language, is requested.

Claim 1 and all claims dependent therefrom have been amended to recite the language “wherein if said primers were used to amplify said reference sequence, the resulting amplified portions of said reference sequence would overlap by less than 5%, and further, wherein said subset of primer pairs may be used for amplifying said target nucleic acid sequence” which is considered vague and indefinite. It is unclear if Applicants’ intend the optional type language (i.e. “if”/“were used”/“may be”) to be included in the claims. Are the primers used to amplify said reference sequence resulting in amplified portions of said reference sequence with less than 5% overlap or not? Is the subset of primer pairs used to amplify said target nucleic acid sequence or not? Clarification of the metes and bounds, via clearer claim language, is requested.

Claims 1, 18, and 19 recite the phrases “target sequence” and “reference sequence” which is confusing. For example, claim 1 a “target sequence” in the preamble, however, the claimed steps recite, “reference sequence”. The instant claim language fails to maintain consistent language terminology and therefore is found confusing. Clarification, via clearer claim language, is requested.

Claims 11, 28, and all claims dependent therefrom recite the phrase “a minimal or substantially minimal number of primer pairs” which remains vague and indefinite. Applicants point to the following for support of the above language:

“Typically the goal of the fourth step is to choose the primer pairs that allow one to amplify all or substantially all of the entire target sequence with reduced sequence amplification overlap and/or minimal or substantially minimal number of primer pairs.” (Paragraph [0032])

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Applicants submit the specification, therefore, makes it clear that it is “preferable to have fewer number of primer pairs” and that “the actual number of primer pairs required to amplify “all or substantially all” of the target sequence depends on several criteria, not the least of which is the length of the target sequence that one wishes to amplify, and the number of primer pairs initially yielded by the initial primer pair selecting step”. This argument is found unpersuasive wherein the criteria (indicated by Applicants’ as several) required for the determination of the actual number of primer pairs (i.e. minimal or substantially minimal number) is absent. The language “minimal or substantially minimal number” implies a criteria or range of values that is considered to be “minimal and substantially minimal number”. Again, Applicants can resolve this issue by particularly pointing out the criteria/range that encompasses “minimal and substantially minimal”. Clarification of the metes and bounds, via clearer claim language, is requested.

Claim 32 is indefinite due to the lack of clarity of the claim language failing to correspond with the preamble. The preamble states that it is “A system that designs primer pairs for amplifying a target nucleic acid sequence”, however, the claim fails to indicate a component(s) that “designs primer pairs”. None of the recited components (processor or computer readable medium) of the system are indicated for designing primer pairs. In such absence it is unclear what component(s) are intended to design primer pairs as recited by the preamble. Clarification of the metes and bounds, via clearer claim language, is requested.

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LACK OF ANTECEDENT BASIS

Claims 15-17 recite the limitation "said computer program" which lacks proper antecedent basis. Claims 1 and 11 (which claims 15-17 depend from) fails to indicate any computer program in the instantly claimed method.

Claims Rejected Under 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7, 9, 11-14, 18-23, 26, 28, 29, and 32 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Harris taken in view of Primer3.

Harris describes an automated sequence (i.e. human, drosophila, etc) annotation and annotation browsing workbench (computer system with processor, memory, storage medium, and display), Genotator, with the additional capability of primer design (claims 1, 22, and 32; Abstract; page 756, right column, lines 19-23; and Figures 1, 5, and 6). The workbench system can search for repeat sequences (such as Alu repeats, which are ubiquitous throughout the human genome; there are also repeat sequences found in the genomes of other organisms) and then masks the repeat sequences (i.e. resulting in a removed reference sequence; repeat regions removed) (claims 1, 7, 22, and 32; page 757, left column, lines 24-30). Additionally, Genotator is linked to several reference databases (claim 23; page 756-757; Figures 5 and 8). To assist the designing of primers for an annotated region of interest Genotator can call Primer3 (primer selection program), wherein the best forward and reverse primers (i.e. minimal primer pairs) are

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printed to the terminal and also indicated in the sequence display (claims 9, 11-14, 18-22, 28, and 32; page 760, left column, lines 10-22). Harris does cite and indicate the linking of primer selection (i.e. Primer3). However, Harris does not describe the details for primer selection.

Primer3 is a computer program that selects primers for amplification of a sequence (i.e. polynucleotide chain reaction) by considering several factors/parameters (page 1-2). For example, the factors include product size (page 6, lines 29-44), primer size (page 7, lines 8-20), primer melting temperature (page 7, lines 21-38), GC content (pages 7-8, lines 39-40 and 1-3, respectively), primer-dimer possibilities (pages 8-9, lines 32-46 and 1-28, respectively), and likelihood of annealing to or amplifying (page 10, lines 24-36) (claims 2-6, 21, 26, 28, and 29). Additionally, primers may not overlap any region (i.e. reduced overlap) specified in the excluded regions of low sequence quality or regions containing repetitive elements (page 5, lines 1-9).

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the invention to practice the automated sequence annotation and annotation browsing workbench (Genotator) as taught by Harris with the primer design method/program in view of Primer3. Harris indicates the additional capability of Genotator for primer design via Primer3 (page 760, left column, lines 10-22).

INFORMATION DISCLOSURE STATEMENT

Several cited references in the 'Information Disclosure Statement', filed 09 January 2002, were previously lined through because of citation to website pages that are presumed to be continually updated and therefore such publicly available information on said website(s) cannot be confirmed. Applicants submit that hard copy print-outs with the dates of printing shown in the lower-right hand corner indicate the dates that such information was publicly available.

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However, this is found unpersuasive. For instance, the cited reference "Long PCR reagents & guidelines" from twod.med.harvard.edu cannot be found at said website; the website is indicated as having been updated on 13 October 2003.

No Claims Are Allowed.

EXAMINER INFORMATION

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 C.F.R. § 1.6(d)). The CM1 Fax Center number is either (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Channing S. Mahatan whose telephone number is (571) 272-0717. The Examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina M. Plunkett, whose telephone number is (571) 272-0549 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

Date:

April 15, 2004

Examiner Initials:

CSM

Marianne P. Allen
MARIANNE P. ALLEN
PRIMARY EXAMINER

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4/15/04